SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION:

Device Generic Name:	Posterior Chamber Phakic Intraocular Lens (PIOL) for Myopic Correction
Device Trade Name:	STAAR Visian ICL™ (Implantable Collamer Lens™); Models MICL12.1, MICL12.6, MICL13.2, MICL13.7
Applicant's Name and Address:	STAAR Surgical Company 1911 Walker Avenue Monrovia, California 91016
Date of Panel Recommendation:	October 3, 2003
Premarket Approval Application (PMA) Number:	P030016
Date of Notice of Approval to Applicant:	December 22, 2005

II. INDICATIONS FOR USE:

The Visian ICL™ is indicated for adults 21-45 years of age:

- to correct myopia ranging from -3.0 diopters to ≤ -15.0 diopters with less than or equal to 2.5 diopters of astigmatism at the spectacle plane;
- to reduce myopia ranging from greater than -15.0 diopters to - 20.0 diopters with less than or equal to 2.5 diopters of astigmatism at the spectacle plane; and,
- with an anterior chamber depth (ACD) 3.00 mm or greater, and a stable refractive history within 0.5 diopter for 1 year prior to implantation.

III. CONTRAINDICATIONS:

The Visian ICL™ is contraindicated in patients:

- With an anterior chamber depth (ACD) < 3.00 mm
- With anterior chamber angle less than Grade II as determined by gonioscopic examination.
- Who are pregnant or nursing
- Who do not meet the minimum endothelial cell density

Endothelial Cell Density

Age	Minimum ECD – ACD ≥ 3.0 mm	Minimum ECD – ACD ≥ 3.2 mm	Minimum ECD – ACD ≥ 3.5 mm
21-25	3875 cells/mm^2	3800 cells/mm^2	3250 cells/mm^2
26-30	3425 cells/mm^2	3375 cells/mm^2	2900 cells/mm^2
31-35	3025 cells/mm^2	2975 cells/mm^2	2625 cells/mm^2
36-40	2675 cells/mm^2	2625 cells/mm^2	2350 cells/mm^2
41-45	2350 cells/mm^2	2325 cells/mm^2	2100 cells/mm^2
> 45	2075 cells/mm^2	2050 cells/mm^2	1900 cells/mm^2

The "Endothelial Cell Density" table indicates the minimum endothelial cell density (ECD) per age group at time of implantation for three different ACD ranges. This table was developed using rates of 2.47%, 2.44% and 2.15% (the upper 90% confidence interval of the average cell loss for eyes with the specified ACD) for the ≥ 3.0 mm, ≥ 3.2 mm, and ≥ 3.5 mm groups, respectively. It sets minimum endothelial cell density criteria as functions of age that should result in at least 1000 cells/mm^2 at 75 years of age. The patient's ECD should be monitored periodically at the physician's discretion.

IV. WARNINGS AND PRECAUTIONS:

The warnings and precautions can be found in the Visian ICL™ labeling.

V. DEVICE DESCRIPTION:

The Visian ICL™ is an intraocular implant manufactured from a proprietary hydroxyethyl methacrylate (HEMA)/porcine-collagen based biocompatible polymer material. The Visian ICL™ features a plate-haptic design with a central convex/concave optical zone and incorporates a forward vault to minimize contact of the Visian ICL™ with the central anterior capsule.

The Visian ICL™ features an optic diameter with an overall diameter that varies with the dioptric power; the smallest optic/overall diameter being 4.9 mm/12.1 mm and the largest

5.8 mm/13.7 mm. All descriptions of optic diameter, overall diameter or Visian ICL™ power refer measurements in BSS unless otherwise noted. The lenses are capable of being folded and inserted into the posterior chamber through an incision of 3.5 mm or less. The Visian ICL™ is intended to be placed entirely within the posterior chamber directly behind the iris and in front of the anterior capsule of the human crystalline lens. When correctly positioned, the lens functions as a refractive element to optically reduce moderate to high myopia

Model Number	Dioptric Power (D)	Overall Diameter (mm)	Optic Diameter (mm)	Haptic Design
MICL12.1	-3.0 to –16.0 D	12.1	4.9- 5. 8	Flat, plate
MICL12.6	-3.0 to –16.0 D	12.6	4.9- 5. 8	Flat, plate
MICL13.2	-3.0 to –16.0 D	13.2	4.9- 5. 8	Flat, plate
MICL13.7	-3.0 to –16.0 D	13.7	4.9- 5. 8	Flat, plate

More detailed information regarding the Visian ICL™ is provided in the Visian ICL™ labeling.

VI. ALTERNATIVE PRACTICES AND PROCEDURES:

The procedures used in the treatment of myopia are spectacles, contact lenses, laser in situ keratomileusis (LASIK), automated lamellar keratoplasty (ALK), radial keratotomy (RK), and photorefractive keratectomy (PRK).

VII. MARKETING HISTORY:

The Visian ICL™ as of the date of the Premarket Approval Application submission has been marketed in over 37 countries to date.

The Visian ICL™ has not been withdrawn from marketing in any of the above countries for any reason relating to the safety and effectiveness of the device or for any other reason.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH:

A total of 526 eyes of 294 subjects were evaluated in the clinical trial to determine the safety of the Visian ICL™.

Anterior subcapsular opacities, not all clinically significant, were observed postop in 14 eyes (2.7%). Seven (50%) of these opacities were first observed within the first postoperative week, 4 (28.6%) between 1 and 6 months postoperatively, and 3 were first observed at 1 year or later postoperatively. Only 2 (0.4% of the total cohort) of the anterior subcapsular opacities progressed to clinically significant opacities while 5 (1%) nuclear opacities were clinically significant. Increase in postop cylinder (>2 D) at 3 years (0.4%). Loss of BSCVA ≥ 2 lines occurred in 4 eyes (0.8%); =2 lines in 6 eyes (1.2%).

The adverse events/complications experienced during the clinical study of the Visian ICL™ (between 1 and 36 months) all occurring in ≤ 1% of cases (cumulative) and included 3 retinal detachments (0. 6%), 2 cases of glaucoma (0.4%), 1 case of elevated IOP > 25 mmHg /> 10 mmHg change from baseline at last visit (0.2%), 1 macular hemorrhage (0.2%) and 1 subretinal hemorrhage (0.2%). Corneal edema and iritis were not reported after the 1 week visit. No cases of macular edema, endophthalmitis, corneal ulcer, corneal haze/edema (after 1 week), hypopyon, hyphema or persistent corneal edema were reported during the study.

Incidence of adverse events/complications (compared with the FDA Grid for cataract extraction and posterior chamber Intraocular Lens (IOL) implantation) and incidence of surgical reinterventions are shown below in Table S1.

Table S1

Adverse Event	Cumulative % (n/N)	FDA Grid %	Persistent (3 Years) % (n/N)	FDA Grid %
Endophthalmitis	0% (0/526)	0.1%	0% (0/526)	---
Hyphema	0% (0/526)	2.2%	0% (0/526)	---
Hypopyon	0% (0/526)	0.3%	0% (0/526)	---
IOL Dislocation	0% (0/526)	0.1%	0 (0/526)%	---
Cystoid Macular Edema	0% (0/526)	3.0%	0% (0/526)	0.5%
Pupillary Block	0% (0/526)	0.1%	0% (0/526)	---
Retinal Detachment**	0.6% (3/526)	0.3%	0% (0/526)	---
Surgical Reintervention	3.1% (16/526)	0.8%	0% (0/526)	---
Corneal Edema (after 1 week)	0% (0/526)	---	0% (0/526)	0.3%
Iritis* (after 1 week)	0% (0/526)	---	0% (0/526)	0.3%
Raised IOP Requiring Intervention	3.8% (20/526)	---	0.4% (2/526)	0.4%
SURGICAL TREATMENTS NOT MONITORED IN FDA GRID				
Refractive Procedures	20/526 (3.9%)	---	---	---
Iris Prolapse Repair	0.2% (1/526)	---	0% (0/526)	---

*There is no FDA Grid Rate for cumulative iritis.

**Comparison should be made to literature for retinal detachment rates for high myopia.

- Retinal detachment rates increase with increasing myopia.[1]
- The risk of retinal detachment within one year of implantation of this device is 0.2%. The risk of retinal detachment for high myopes following implantation is more than 10 times the risk without surgery, i.e., greater than 10 fold the background rate of retinal detachment for high myopes (greater than minus 3 diopters). 5.0% in myopes >- 6 D[2] and 0.8% to 7.5 % in pseudophakic eyes with high axial myopia.[3]

[1]Ogawa A, Tanaka, M., The relationship between refractive errors and retinal detachment. Jpn J Ophthalmolo 32;310:1988.

[2]Dellone-Larkin G, Dellona CA. Retinal detachment. Available at: http://www.emedicine.com/emerg/topic504.html

[3]Jacobi F, Hessemer V. Pseudophakic retinal detachment in high axial myopia. J Cat Ref Surg 23;1095:1997.

Refractive procedures include: AK and LASIK

Surgical reinterventions (see Table S2 below) were not shown to have an impact on safety or efficacy. Surgical reinterventions occurred in 3.1% of cases.

Table S2

Visian ICL™ Related Additional Surgery	**n**	**%***
Visian ICL™ Repositioning	4	0.8%
Visian ICL™ Replacement, then Removal	1	0.2%
Visian ICL™ Replacement	8	1.5%
Visian ICL™ Removal	3	0.6%
TOTAL	16	3.1%

*Total Study Cohort (N= 526)

Other Complications:

Postoperatively IOP > 25 mmHg during follow-up or an increase of > 10 mmHg over preoperative took place in 5 cases through 3 years (only 1 persisted at last visit); 1.4% of the Visian ICL™ PMA Cohort. Only 2 cases (0.4%) in the entire cohort were diagnosed with ocular hypertension and started on pressure lowering medication. No cases (0.0%) in this study exhibited optic nerve or visual field changes characteristic of glaucoma.

IX. SUMMARY OF PRECLINICAL STUDIES:

STAAR Surgical complied with all relevant required preclinical testing outlined in the Agency's "Refractive Implants Guidance for Investigational Device Exemption (IDE) and Premarket Approval Application (PMA) Applications"-August 1, 2000. Non-clinical testing demonstrated the safety and effectiveness of the Visian ICL™. Summaries of the non-clinical test conducted are listed below.

Biocompatibility Testing

The Visian ICL™ is manufactured from the same material using the same manufacturing processes and facilities as the Collamer Intraocular Lens previously approved under PMA P990013. All required testing confirmed that the Collamer material is biocompatible, as shown below in Table S-3.

Table S-3
Biocompatibility Testing Summary

BIOCOMPATIBILITY TESTING-TYPE	METHODOLOGY/TESTING RESULTS
Cytotoxicity-MEM Elution	Results: No evidence of lysis or cytopathic effects.
Cytotoxocity Agar Overlay-Direct Contact	Results: No evidence of cell lysis (non-cytotoxic).
Cytotoxicity Agar Overlay-Extract	Results: No evidence of cell lysis (non-cytotoxic).
Acute Systemic Toxicity	Results: No signs of toxicity.
Intracutaneous Toxicity	Results: No evidence of irritation or toxicity.
Intramuscular Implantation	Results: Test sample reaction not significant compared to USP negative control.
Ocular Irritation	Results: No evidence of irritation in test and control eyes.
Hemolysis-Direct Contact *(In-Vitro)*	Results: No evidence of red blood cell lysis.
Hemolysis Test-Extract *(In-Vitro)*	Results: No evidence of red blood cell lysis.
Inhibition of Cell Growth-One Point Assay	Results: All samples non-inhibitory.
Guinea Pig Maximization (Sensitization)	Results: Samples were found to be non-irritating.
Ames Mutagenicity	Results: Samples found to be non-mutagenic.
Sister Chromatid Exchange	Results: No relevant increase in SCE was observed at 500 and 1000 µl/ml concentrations used in study; Extract of Collamer IOL considered negative for inducing SCE in CHO cells with/without metabolic activation
Chromosomal Aberrations	Results: Collamer IOL considered negative for inducing chromosomal aberrations in CHO cells with/without metabolic activation.
Rabbit Implants (6 & 12 months)	Results: Lenses appeared to be well tolerated in rabbit eyes and caused no inflammatory reaction under histopathologic evaluation.
LAL Kinectic-Chromogenic Assay	Results: Test article determined to be non-pyrogenic.
Systemic Antigenicity	Results: Non-significant reactions; test article extract considered non-mutagenic.
Complement Activation	Results: No potential for anaphylaxis if test material not in direct contact with vascular system

Corneal Endothelial Touch Study	Results: Test group showed lower overall percentage of cell damage when compared to PMMA control.

Mechanical, Physical and Optical Testing

Table S-4
Mechanical/Physical/Optical Tests

Fourier-Transform Infrared	Consistent with molecular structures
Light Transmission	90% ± 5% at 500 nm
UV Visible Spectroscopy	10% transmission @ 387 nm
Refractive Index @ 35 °C	1.440 (in BSS)
Specific Gravity	1.21

Additional testing performed with acceptable results included: differential scanning calorimetry, USP Physico-Chemical, elongation, tensile strength, durometer, photostability, folding/resolution, swell index, gel permeability chromatography, optical stability, modular transfer function, surface evaluation, slit lamp discoloration and amino acid/protein identification analysis.

Exhaustive Extraction

Testing showed that the Collamer material has an acceptable level of extractable materials. Specific testing included:

Table S-5
Extraction Testing

Exhaustive Extraction Isopropyl Alcohol and Water	Results: In IPA: No measurable extractable In Water: 0.01% of 2-Hydroxyethylmethacrylate
Accelerated Leachability Saline	5.6 ± 3.0ppm chromophore extracted

Nd:YAG Testing

Testing of the Collamer material with the Nd: YAG resulted in no release of toxic materials after Nd: YAG exposure.

Microbiological Testing

The following information summarizes the tests performed to verify the effectiveness of the autoclave sterilization cycle. Steam sterilization leaves no toxic residues. The Collamer optic is unaffected by the temperatures of steam sterilization. Testing was performed to measure the bioburden (number of viable microorganisms present prior to sterilization) of lenses as one aspect in the evaluation and development of sterilization

process. The sterilization process itself is designed to provide a high level of assurance that intraocular lenses achieve a sterility assurance level of 10^{-6}.

1. The qualification for the sterilization process was based on the overkill method. The sterilization process challenge device was *Bacillus stearothermophilus* (10^6 spores) with a minimum D-value of 2.8 minutes. Comparative resistance of the process challenge device and the naturally occurring product bioburden show that the challenge device is more resistant to the sterilization process.

2. Results of sterility testing for both the process challenge device and the product showed no positives for any of the half or full cycles.

3. Bacterial Endotoxins - The results of Pyrogen testing using the USP LAL Bacterial Endotoxin Test demonstrated that the lenses meet the FDA limits for endotoxins on medical devices (0.5 EU/ml).

4. Shelf-life - The sponsor has adequate data to justify a shelf-life expiration date of 24 months on the basis of package integrity and physical stability.

X. SUMMARY OF CLINICAL STUDIES:

An overview of the Visian ICL™ moderate to high myopic IDE (IDE G960218) clinical study is provided below:

STUDY OBJECTIVE:

The objective was to assess the safety and efficacy of the Visian ICL™ for the correction of moderate to high myopia.

STUDY DESIGN:

The study was a prospective, multi-center, one arm cohort study where the primary control was the preoperative state of the treated eye (i.e., comparison of pretreatment and post-treatment visual parameters in the same eye).

Inclusion Criteria:

- Moderate to high myopia (-3.0 D to -20.0 D measured as spherical equivalent of the manifest refraction).
- Cylindrical portion of the manifest refraction $\leq$ 2.5 D.
- Stable refraction for the last 12 months as documented by previous clinical records.
- Spherical equivalent of the manifest refraction has progressed at a rate of 0.5 D or less during the year prior to the baseline exam.
- Correctable to at least 20/100 in treated eye.
- Ages 21 to 45 years of age.
- Signed written informed consent form.
- Willingness to return for scheduled follow-up examinations after surgery.

Exclusion Criteria:

- History of/or clinical signs of iritis/uveitis in either eye.
- Diabetic retinopathy in either eye.
- Glaucoma in either eye.
- History of previous ocular surgery in the treated eye with the exception of previous AK.
- Blind in the fellow eye.
- Myopia less than -3 D or more than -20 D.
- Cylinder greater than 2.5 D.
- Unstable refraction as defined in Inclusion Criteria.
- Serious (i.e., life threatening) non-ophthalmic disease which might preclude study completion.
- Progressive sight-threatening disease other than myopia.
- Diagnosis of ocular hypertension.
- Insulin-dependent diabetes.
- Pseudoexfoliation with or without glaucoma and narrow angles (less than Grade II) as determined by gonioscopic exam.
- Fellow eye that is contact lens intolerant.

Demographics

The Visian ICL™ was evaluated in a prospective nonrandomized study of 526 eyes of 294 subjects, 470 of which were followed for 1 year and 369 followed for 3 years. Study Cohort demographics are as follows:

Table S-6
Demographics: 526 Eyes of 294 Subjects

Age	Race		Gender	
	Black	2.0%		
Average: 36.55 ± 5.8 years	Caucasian	84.7%	Female	60.5%
Range: 22 to 45 years	Hispanic	7.8%	Male	39.5%
	Other	5.4%		

There was no difference between male and female for major safety parameters (≥ 2 lines loss BSCVA, Secondary Surgical Intervention, as opacity). There was no difference between male and female for major efficacy parameters (Uncorrected Corrected Visual Acuity (UCVA)) 20/20 or better at 36-month, UCVA 20/40 or better at 36 month, patient satisfaction, predictability within 0.5 D at 36 month). Analysis reveals preponderance toward the female gender (60.5%), although there was no difference in safety and effectiveness of the device based on gender.

Data Analysis and Results

Preoperative Characteristics

Table S-7 provides a summary of preoperative uncorrected visual acuity. Emmetropia was targeted in 67.7% of all PMA Cohort cases. One hundred and twelve (21.3%) eyes had preoperative myopia of ≥ 7 D, 174 (33.1%) had > 7 D to -10 D, 188 (35.7%) had > 10 D to 15 D, and 52 (9.9%) had > 15 D.

Table S-7
Preoperative UCVA Characteristics

UCVA 20/40 or better	0% (0/0)
UCVA 20/80 or better	0% (0/0)
Worse than 20/200	99.4% (523/526)

Postoperative Results

Accountability

The clinical study protocol prospectively identified the following visit schedule: 1 day, 1 week, 1 month, 3 months, 6 months, 12 months, 24 months. During the course of the Visian ICL™ clinical investigation, in accordance with a request from FDA, a 36 month postoperative visit was added. A summary of the accountability for the 526 eyes in the Visian ICL™ PMA Cohort through 36 months is provided in Table S-8. The overall accountability with postoperative follow-up visit requirements (% Accountability) was between 89.7% and 100% through the 24 month follow-up examination. At 12 and 24 months after Visian ICL™ implantation, 89.7% and 90.6%, respectively of the eyes eligible for evaluation were examined. The proportion of cases examined at 2 or more years totaled 96.6%. At 36 months postoperatively, the % Accountability was 77.2%, which exceeds the FDA target of 70% in the U.S. Refractive Implants Guidance for Investigational Device Exemptions (IDE) and Premarket Approval (PMA) Applications (8/00).

All treated eyes were included in the safety and efficacy cohort however for the efficacy cohort, data concerning the 4 eyes discontinued because the Visian ICL™ was removed was not included following the removal. Similarly the data on the 20 cases (3.8%) that underwent secondary refractive procedures was only included up to the point of the secondary procedure.

TABLE S-8

ACCOUNTABILITY

The Implantable Collamer Lens for Myopia

526 Eyes Treated of 294 Patients

	1 Day	1 Week	1 Month	3 Months	6 Months	12 Months	24 Months	36 Months
Available for Analysis	526	507	511	487	482	470	454	369
Discontinued (ICL Removals)**	0	0	0	0	0	0	1	4
Missed Visit/CRF Not Received	0	19	15	36	40	44	33	76
Not yet eligible for the interval	0	0	0	1	1	2	24	44
Lost to Follow-up***	0	0	0	2	3	10	14	33
Available for Analysis	526	507	511	487	482	470	454	369
(Enrolled-Discontinued-Not yet eligible)	526	526	526	525	525	524	501	478
= % Accountability	**100.0%**	**96.4%**	**97.1%**	**92.8%**	**91.8%**	**89.7%**	**90.6%**	**77.2%**

*Cases seen 2 yrs or later is 480 (96.58%).

**Cumulative total number of eyes discontinued is 4.

***Cumulative total number of eyes lost to follow-up is 33.

****As of 2/25/2003 (date database closed).

Visual Acuity

The postoperative results demonstrated that the Visian ICL™ can provide full correction for high myopia up to -15D and only partial correction up to -20D. The visual acuities at 1 and 3 years are described in the following tables:

Table S–9
UCDVA = Uncorrected Distance Visual Acuity, Snellen
(Where emmetropia was the goal (± 0.50 D) and Pre-op Best Spectacle Corrected Visual Acuity (BSCVA) better than or equal to 20/20)

	1 Year	3 Year
N	240	189
20/20 or better	65.4%	59.3%
20/40 or better	96.7%	94.7%
20/80 or better	99.6%	98.9%
Worse than 20/80	0.4%	1.1%

Table S–10
UCVA* by Preoperative MRSE

Myopia Group	Exam Interval	N	20/20 or Better	20/40 or Better
Study Cohort	1 Week	259	49.8%	91.9%
	1 Month	262	56.5%	95%
	3 Months	251	63.7%	96.4%
	6 Months	248	60.9%	96.4%
	1 Year	240	65.4%	96.7%
	2 Year	228	59.6%	93.4%
	3 Year	189	59.3%	94.7%
≤ -7 D	1 Year	80	76.3%	98.8%
	2 Year	74	70.3%	97.3%
	3 Year	58	72.4%	98.3%
> -7 D to -10 D	1 Year	100	70.0%	96.0%
	2 Year	98	64.3%	94.9%
	3 Year	83	62.7%	92.8%
> -10 D to -15 D	1 Year	60	43.3%	93.7%
	2 Year	56	37.5%	95.0%
	3 Year	48	37.5%	93.8%
> -15 D	1 Year	0	NA%**	NA%**
	2 Year	0	NA%**	NA%**
	3 Year	0	NA%**	NA%**

*Eyes with Preoperative BSCVA 20/20 or Better and Emmetropia Targeted Correction
** No Eyes > -15 D group with this Preop Status

Table S–11
BCDVA = Best Corrected Distance Visual Acuity, Snellen
(Eyes with Preoperative BCVA 20/20 or better)

	1 Year	3 Year
N	321	253
20/20 or better	95.6%	96.4%
20/25 or better	99.7%	100%
20/40 or better	100%	100%

Table S–12
BCDVA = Best Corrected Distance Visual Acuity, Snellen, By Preop Myopia
(Eyes with Preoperative BCVA 20/20 or better)

Preop Myopia Group	Exam Interval	N	20/20 or better	20/25 or better	20/40 or better
≤ -7 D	1 Year	87	95.4%	98.9%	100%
	2 Year	81	96.3%	98.8%	100%
	3 Year	63	98.4%	100%	100%
> -7 D to -10 D	1 Year	136	97.1%	100%	100%
	2 Year	133	94.7%	100%	100%
	3 Year	109	100%	100%	100%
> -10 D to -15 D	1 Year	91	94.5%	100%	100%
	2 Year	87	94.3%	98.9%	100%
	3 Year	77	90.9%	100%	100%
> -15 D	1 Year	7	85.7%	100%	100%
	2 Year	5	100%	100%	100%
	3 Year	4	75%	100%	100%

Table S–13
Spherical Equivalent (Target Variance) Distribution

	1 Year	3 Year
N	455	363
± 0.50 D	69%	68.3%
± 1.0 D	91.6%	89.5%

Stability

The refraction was stable with 97.6% of eyes achieving less than or equal to ± 1.0 D of shift at 3 years. The proportion of eyes achieving less than or equal to ± 1.0 D of shift at 3 years by preoperative myopia group was as follows; 100% for ≤ -7 D, 99.1% for > -7 D to 10 D, 95.9% for > -10 D to 15 D, and 95.7% for > -15 D.

Table S–14
Manifest Refraction Spherical Equivalence (MRSE)
Change between Visits

	6 Month to 1 Year	1 Year to 2 Year	2 Year to 3 Year
N	424	413	337
± 0.25 D	75.5%	76.8%	75.1%
± 0.5 D	91.0%	89.8%	90.2%
± 1.0 D	97.6%	97.6%	97.6%
> 1.0 D	2.4%	2.4%	2.4%

Table S–15
Manifest Refraction Spherical Equivalence (MRSE)
By Preoperative Myopia Group- Consistent cohort
Change between Visits

Myopia Group	Exam Interval	N	± 0.5 D	± 1.0 D	Mean Change Per Month
≤ -7 D	6 mo to 1 Year	54	98.1%	100%	0.02 D
	1 Year to 2 Years		94.4%	94.4%	0.02 D
	2 Years to 3 Years		94.4%	100%	0.01 D
> -7 D to -10 D	6 mo to 1 Year	110	88.2%	98.2%	0.03 D
	1 Year to 2 Years		90.0%	100%	0.02 D
	2 Years to 3 Years		94.5%	99.1%	0.01 D
> -10 D to -15 D	6 mo to 1 Year	98	93.9%	98.0%	0.04 D
	1 Year to 2 Years		92.9%	99.0%	0.02 D
	2 Years to 3 Years		85.7%	95.9%	0.02D
> -15 D	6 mo to 1 Year	23	91.3%	95.7%	0.04 D
	1 Year to 2 Years		82.6%	95.7%	0.02 D
	2 Years to 3 Years		78.3%	95.7%	0.03 D

Endothelial Cell Density

Endothelial cell density was performed using a single reading center to minimize standard deviations inherent in this test method. A percent change from baseline to 3 years of 8.9% (SD 8.5%), and from baseline to 4 years of 10.6% (SD 9%) was found. Endothelial cell loss over time in patients with extremely high myopia is unknown.

Mean EC density results are shown in the following table:

Table S–16
Mean Endothelial Cell Density Results

Visit	Mean	Standard Deviation	90% Confidence Limits
Pre-op	2657	286	2625 to 2689
6 Months	2571	337	2534 to 2608
1 Yr	2544	352	2508 to 2580
2 Yr	2476	356	2438 to 2514
3 Yr	2434	359	2393 to 2475
4 Yr	2387	399	2327 to 2447

The available data from the clinical study indicates a continual steady loss of endothelial cell density of -2.2% per year and this rate has not been established as safe.

The following table provides the predicted percent endothelial cell loss, by year, for an individual patient with pre-operative endothelial cell density equal to the mean level in the clinical study. For this individual patient and time, there is 90% confident that the endothelial cell loss will be between the lower and upper prediction interval bounds. The entries in this table are calculated assuming a constant linear loss in endothelial cell density from three months after the procedure.

Table S–17
Predicted Endothelial Cell Loss

Years from procedure	Predicted Percent Cell Loss	90% prediction interval	
		Lower	Upper
3 months	3%	2.5%	3.8%
1	4.6%	3.8%	5.7%
2	6.6%	5.5%	8.4%
3	8.7%	7.2%	11.1%
4	10.8%	8.9%	13.7%
5	12.8%	10.5%	16.4%
10	23.2%	18.7%	30.2%
15	33.6%	26.5%	44.4%
20	44%	34.1%	59.1%
25	54.3%	41.5%	74.2%
30	64.7%	48.6%	89.5%
35	75%	55.6%	100%
40	85.4%	62.4%	100%
45	95.8%	69.1%	100%
50	100%	75.8%	100%
55	100%	82.3%	100%
60	100%	88.8%	100%

Optical Visual Symptoms

The following table reports the subjective optical visual patient symptoms reported during this clinical study after Visian ICL™ implantation compared to before the Visian ICL™ surgery:

Table S–18
Subjective Patient Symptoms- Compared to Pre-op

Patient Symptom	Improved at 3 Years	No Change at 3 years	Worsened at 3 Years
Glare	12.0%	78.3%	9.7%
Halos	9.1%%	79.4%	11.4%
Double Vision	1.1%%	97.2%	1.7%
Night Vision	12%%	76.0%	12.0%
Night Driving Difficulties	13.7%	76.1%	10.1%

Additional Clinical Outcomes:

Predictability of intended refraction

The following table provides predictability of intended refraction (± 0.50D and ±1.0D) for all eyes and by the level of preoperative refraction.

Table S–19

MRSE *vs.* Intended Target[1] by Pre-op MRSE

Lens Group	Exam Interval	*N*	± 0.50 D	± 1.0 D	± 2.0 D
Study Cohort	1 Week	501	64.7%	87.4%	97.2%
	1 Month	506	68%	87.9%	97.8%
	3 Months	485	63.9%	88.7%	97.9%
	6 Months	479	66.8%	88.9%	98.1%
	1 Year	455	67.7%	90.3%	98.2%
	2 Year	443	66.1%	90.1%	98%
	3 Year	363	67.5%	88.2%	98.1%
New Calculation Method[3]	3 Year	363	70.0%	89.3%	98.3
≤ -7 D Cohort	3 Year	72	84.7%	97.2%	100%
New Calculation Method[3]	3 Year	72	86.1%	97.2%	100%
> -7 to -10 D Cohort	3 Year	131	71.0%	93.1%	100%
New Calculation Method[3]	3 Year	131	70.2%[2]	92.4%[2]	100%
> -10 D to -15 D Cohort	3 Year	130	64.6%	86.2%	98.5%
New Calculation Method[3]	3 Year	130	70%	88.5%	99.2%
> -15 D Cohort	3 Year	30	23.3%	53.3%	83.3%
New Calculation Method[3]	3 Year	30	30%	60%	83.3%

[1]All Study Cohort Eyes
[2]Note % lower with new Power Calculation Method
[3]The new calculation method was used to correct for a change in power labeling to allow standard phakic IOL power formulas to be used without modification. It is a theoretical calculation only.

The following table shows the UCVA for all eyes and by the level of preoperative refraction for all eyes implanted that were targeted for emmetropia and had a BSCVA of 20/20 or better preoperatively.

Subjective Quality of Vision

Subjective quality of vision was assessed by means of a questionnaire administered to all patients.

Table S–20
Subjective Quality of Vision-All Eyes

Quality of Vision Grading	Pre-op	36 months
Very Good/Excellent	288 (55%)	267 (77%)
Good	175 (33.4%)	59 (17.1%)
Poor/Very Poor	61 (11.6%)	20 (5.8%)

Subjective Patient Symptoms Stratified by Optic Diameter

Subjective patient symptoms were stratified into 4 groups based on the optic diameter: 4.9 mm, 5.2 mm, 5.5 mm and 5.8 mm. Glare was absent/mild in 82.4% of patients in the 4.9 mm, 90.3% in the 5.2 mm, 91.8% in the 5.5 mm and 89.9% in the 5.8 mm groups. Marked/severe glare occurred in 3.3% of eyes with the 4.9 mm, 2.8% with the 5.2 mm, 4.1% with the 5.5 mm and 1.4% with the 5.8 mm at 36 months postoperatively.

The incidence/severity of halos increased, the smaller the optic diameter. Halos were absent/mild in 80.2% of patients in the 4.9 mm, 87.3% in the 5.2 mm, 89.8% in the 5.5 mm and 87.8% in the 5.8 mm. Marked/severe halo was dependent upon the Visian ICL™ optic diameter and was 9.9% with the 4.9 mm, 2.8%with the 5.2 mm, 4.1% with the 5.5 mm and 1.4% with the 5.8 mm.

Double vision was absent in all eyes with the 5.8 mm optic diameter. Double vision was reported as absent in 95.6% of the patients with the 4.9 mm, 98.6 with the 5.2 mm, and 98.0% with the 5.5 mm at 36 months.

The incidence of marked/severe night driving difficulties negatively correlated with the optic diameter. Marked/severe night driving difficulties was reported in 16.7% of eyes in the 4.9 mm group compared to 0% with the 5.8 mm. Night driving difficulties were absent/mild in71.1% of eyes using the 4.9 mm, 83.8% with the 5.2 mm, 85.4% with the 5.5 mm, and 91.9% with the 5.8 mm.

A similar trend between the subjective symptom and the 36-month follow-up shows a negative correlation between the incidence/severity of night vision difficulties and the optic diameter. No cases of marked/severe night vision difficulties occurred with the 5.8 mm. Subjective night vision difficulties 36 months after Visian ICL™ insertion were absent/mild in 73.6% of eyes with 4.9 mm, 84.7% with the 5.2 mm, 83.7% with the 5.5 mm, and 90.6% with the 5.8 mm.

XI. CONCLUSIONS DRAWN FROM THE CLINICAL STUDY:

Risk Benefit Analysis

The Visian ICL™ is surgically implanted in the eye to correct myopia. The lens may eliminate the need for spectacle or contact lenses for some patients. The risks associated with the eye surgery and this lens includes: retinal detachments, cataract, endophthalmitis, raised intra-ocular pressure, uveitis and corneal decompensation (typically related to endothelia cell loss). It is reasonable to conclude that the benefits of use of the devic e for the target population outweigh the risk of illness or injury when used as indicated in accordance with the directions for use.

Safety

Visian ICL™ rates are comparable to or lower than the rates associated with the historical control population of standard posterior chamber monofocal IOLs with the following exceptions: retinal detachment and surgical reinterventions. The 3-year data from the clinical study indicates a continual steady loss of endothelial cells of -2.2% per year and this rate has not been established as safe. If endothelial cell loss continues at the rate of 2.2% per year, 35% of patients are expected to lose 50% of their corneal endothelial cells within 25 years of implantation. The long term-term effect on the cornea's health of a 50% loss in corneal endothelial cells is unknown. However, if too many cells are lost the patient may need a corneal transplant. Therefore, it is very important that the patient's endothelial cell density is periodically monitored.

Effectiveness

The Visian ICL™ met or exceeded the target effectiveness criteria for refractive stability, uncorrected visual acuity, best corrected visual acuity and refractive predictability.

XI. PANEL RECOMMENDATION:

At an advisory meeting held on October 3, 2003, the Ophthalmic Device Panel recommended the PMA for the Visian ICL™ be approved subject to the following conditions:

1. Changes in the indications for use to include:

    a. restricting the use of the device to patients with anterior chamber depth of 3 mm and greater; and,

    b. indicating the device for the reduction of myopia in patients with -15 to -20 diopters of myopia.

2. Recommending that 4 and 5 year endothelial cell density and rate of cataract formation data be collected in post market studies.

3. revisions to both patient and physician labeling.

4. training.

XII. CDRH DECISION:

The Center for Devices and Radiological Health (CDRH) disagreed with the Ophthalmic Devices Panel's October 3, 2003 approval with conditions recommendation for the following reasons: (1) FDA did not believe that the ECD losses up to three years support the safety and effectiveness of the device, rather, FDA believed four year data should be collected prior to approval of the PMA, in order to confirm the trend towards a decreased rate of ECD loss at four years. (2) the sponsor had unresolved inspectional issues; and (3) FDA had concerns regarding the power calculation. These issues were outlined in our November 26, 2003 not approvable letter. The applicant has adequately addressed these concerns. Also, the applicant has agreed to the following: (1) continue post operative follow-up of the PMA cohort's corneal endothelial cell loss out to five years and provide yearly reports to assess long term safety; (2) conduct a 5-year postapproval study of the adverse events per the protocol outlined in Amendment 18. The study will entail enrollment of 5,000 patients within the United States with the goal of obtaining 5-year follow-up on 2,000 patients to collect safety information and estimate the safety event rates for the Visian ICL™ market in contrast to the well-controlled clinical study environment. The following events/complications will be assessed: cataract formation, corneal decompensation, persistent elevated intraocular pressure (more than 3 months) requiring medication or surgical intervention, retinal detachment, chronic uveitis and secondary surgical interventions (e.g., lens exchange, lens explantation, Visian ICL™ repositioning); and (3) conduct a pre- and post-operative axial length measurement sub-study as outlined in Amendment 18 to determine whether the Visian ICL™ effects this measurement.

FDA issued an approval order on December 22, 2005 (correction letter January 4, 2006). The applicant's manufacturing facility was inspected and was found to be in compliance with the Quality System Regulation (21 FR 820).

Expedited review status was granted on May 8, 2003 for the following reason: we believe that the Visian ICL™ for myopia may provide a clinically meaningful advantage over existing technology in terms of increased effectiveness for patients with high myopia.

XIII. APPROVAL SPECIFICATIONS:

Directions for Use: See labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions and Adverse Events in the labeling.

Post-Approval Requirements and Restrictions: See approval order.